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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/327,750	06/07/1999	TAKA-AKI SATO	59131/JPW/AK	5864

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EXAMINER

LANDSMAN, ROBERT S

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/327,750	SATO, TAKA-AKI	
	<b>Examiner</b>	<b>Art Unit</b>	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on 12 January 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 134-146 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 134-146 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

## DETAILED ACTION

Upon reviewing the claims, the Examiner has determined that not all issues were addressed in the Final Office Action dated 10/16/03. Therefore, the finality of that action is withdrawn and prosecution on the merits continues.

### ***1. Formal Matters***

- A. The amendment dated 1/12/04 has been entered into the record.
- B. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

### ***2. Specification***

- A. The objection to the specification regarding new matter has been withdrawn in view of Applicants' arguments that, in response to the Office Action of November 01, 2002, a letter over the Applicants' signature was submitted which states that the sequence listing does not contain any new matter. The Examiner apologizes for this oversight.

### ***3. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement***

- A. Claims 134, 135, 137-142 and 144-146 remain rejected under 35 USC 112, first paragraph, for the reasons already of record on page 3 of the Office Action dated 10/16/03. Applicants argue that the artisan would be able to identify which proteins can bind to p75 and that apoptosis only occurs when NADE and p75 are expressed together. Applicants also argue that various domains of NADE are known and the region which interacts with p75 is also known. Applicants argue that Figure 1H discloses mouse and other homologs of NADE. These arguments have been considered, but are not deemed persuasive.

While it may be true that Applicants have identified residues of the NADE of the invention required to bind to p75, and have determined that specific regions of the protein are required for NADE interaction with p75, Applicants have only enabled one NADE protein. While Figure 1H does show other proteins which are homologous to the protein of the invention, it is not clear, nor has it been demonstrated, that these proteins are NADE proteins which interact with p75. These proteins are not highly homologous to the protein of the present invention, nor, due to this low homology, can it be determined where the p75 binding domains are on these proteins, nor where the ubiquitination sequences

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are. Furthermore, due to this low homology, it is not clear that the leucines are, in fact, part of a leucine-rich NES. The same is true with Figure 1A.

Therefore, the breadth of the claims remains excessive. Furthermore, Applicants provide guidance and a working example of only one NADE, therefore, it is not predictable to the artisan how to make, or identify other NADE proteins which interact with p75. For these reasons, the Examiner maintains that undue experimentation is required to practice the invention as claimed.

B. Claims 134-136 and 138-146 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of determining whether an agent decreases apoptosis using the NADE of the present invention in vitro, does not reasonably provide enablement for the use of this method in vivo, or for the use of this method in intact cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

At least claim 137 recites that the claimed method is limited to use in vitro, implying that the claims not reciting 'in vitro' have an intended in vivo use. Applicants have not provided any guidance or working examples of the use of the claimed method in vivo, nor would it be predictable to the artisan how to practice this method in vivo.

#### ***4. Claim Rejections - 35 USC § 112, first paragraph – written description***

A. Claims 134, 135, 137-142 and 144-146 remain rejected under 35 USC 112, first paragraph, for the reasons already of record on page 3 of the Office Action dated 10/16/03. Applicants argue that they have identified numerous embodiments of NADE. They argue that the specification defines NADE proteins as hydrophilic and acidic and possess, in addition to their binding site for the p75 neurotrophin receptor cell death domain (SEQ ID NO:1), two significant motifs: the leucine-rich nuclear export signal (NES) and ubiquitination sequences. NADE proteins bind to the cell death domain of p75, specifically to the amino acid residues 338-393, with the C-terminus of NADE being a necessary component of the interaction. In addition, the specification discloses various species of human, mouse and rat NADE, as set forth in SEQ ID NOs:12-13 and SEQ ID NOs:30-39, which illustrate these specific features.

As stated above, while it may be true that Applicants have identified residues of the NADE of the invention required to bind to p75, and have determined that specific regions of the protein are required for NADE interaction with p75, Applicants have only adequately described one NADE protein. While Figure 1H does show other proteins which are homologous to the protein of the invention, it is not clear, nor has

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it been demonstrated, that these proteins are NADE proteins which interact with p75. These proteins are not highly homologous to the protein of the present invention, nor, due to this low homology, can it be determined where the p75 binding domains are on these proteins, nor where the ubiquitination sequences are. Furthermore, due to this low homology, it is not clear that the leucines are, in fact, part of a leucine-rich NES. The same is true with Figure 1A.

B. Claims 134-136, 138-146 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims read on a method of identifying agents which decrease apoptosis by the use of an in vivo method. However, the specification does not provided any written description on how to practice this method in vivo.

#### ***5. Claim Rejections - 35 USC § 112, second paragraph***

A. The rejection of claims 134, 135, 137-142 and 144-146 under 35 USC 112, second paragraph, have been withdrawn in view of Applicants' arguments that NADE proteins are defined in the claims and specification.

#### ***6. Conclusion***

A. No claim is allowable.

#### ***Advisory information***


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.  
Patent Examiner  
Group 1600  
April 05, 2004

  
ROBERT LANDSMAN  
PATENT EXAMINER